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Editorial

Thinking like pediatricians to prevent pneumococcal disease in adults

Pensando como pediatras para prevenir la enfermedad neumocócica en adultos



In this issue of EIMC, Serrano-Tomás et al.,¹ publish a retrospective observational study on invasive pneumococcal disease (IPD) in a university teaching hospital in Madrid, through January 2019 to December 2021. The title of the work includes a crucial question: Are we using pneumococcal vaccine correctly? As the authors conclude, the answer is “no”, since adherence to pneumococcal vaccination was low in the patients included in the study.

In total, 103 patients with IPD were identified (median age 71 years), with only 4 children. Ninety-five percent (98/103) of the patients had risk factors for IPD (mainly chronic cardiopulmonary disease and smoking) and 30 of them had also high-risk conditions, such as chronic kidney disease, liver cirrhosis, previous history of IPD and hematopoietic stem cell transplantation (HPSCT). Almost 20% of the patients (29% in those with high-risk conditions) died within one month of diagnosis.

A fact that prompts reflection is that only 10.5% of adults with IPD who met criteria – by age or underlying conditions – for pneumococcal vaccination had received a vaccination schedule appropriate to their situation. Specifically, less than 15% of adults belonging to risk groups had received a suitable vaccination schedule, and the percentage dropped to 6.6% (2/30) in those patients who suffered from high-risk conditions.

Considering the above, a question is mandatory: Why is vaccination coverage against pneumococcus so low in adults, despite the existence of pneumococcal vaccines that have proven to be effective and with an excellent safety profile? There is probably no single answer, but a lack of perception about the severity of pneumococcal adult infections, both by patients and health workers, seems evident.

The risk for pneumonia and IPD is higher in the elderly and those people with comorbidities such as chronic obstructive pulmonary disease, coronary artery disease, heart failure, diabetes mellitus, chronic autoimmune diseases, chronic kidney disease, malignant diseases, and other immunosuppressed states.² In a study including over 14,000 IPD cases, the odds ratio (OR) for IPD in individuals with chronic comorbidities or immunosuppression was 2.5 and 5, respectively, compared to individuals without any of these conditions. Other risk factors such as inflammatory polyarthropathies, connective tissue diseases, and neurological diseases have been also identified in the same study.² The increased risk for pneumo-

coccal infections is extraordinarily high in immunocompromised patients, ranging from 8 to 55 times for pneumonia and from 30 to 80 times for IPD, depending on the type of immunocompromise.³

Every year in Spain there are more than 50,000 hospitalizations due to pneumococcal infections with a 14% case fatality rate (CFR), which yields a figure of 7000 deaths per year.⁴ Hospitalizations occur mainly in people over 65 years of age, CFR increasing with age. It has been estimated that the annual cost of these hospitalizations is 359 million euros.⁴ A high CFR in IPD and pneumococcal pneumonia has been confirmed in several studies.^{5–7}

Numerous epidemiological studies have shown that cardiovascular complications and stroke are some of the factors contributing to this high CFR. The risk of serious cardiovascular complications increases in patients admitted for IPD or pneumococcal pneumonia and up to 10–30% of them will suffer a worsening or new appearance of a cardiac arrhythmia, congestive heart failure or myocardial infarction.^{8,9}

Nevertheless, the impact of pneumococcal infections goes beyond the high mortality rate and acute consequences of the infection, since patients hospitalized for IPD and/or pneumococcal pneumonia will maintain a significant increase in the risk of any cause death that could last from several months to 10 years, even adjusting for age or the presence of comorbidities.^{5–7} Up to 25–40% of patients will die within 5 years of suffering from pneumococcal pneumonia^{7,10} and more than 80% of those who die will do so sooner than expected, according to their life expectancy.¹⁰

Among the factors that increase the risk of death in the long term, the presence of comorbidities^{7,10} and cardiopulmonary events stand out.⁸ Immunosenescence in older people, a state characterized by chronic increased inflammation and immune deficits in both innate and adaptive immunity, could also contribute to this increase in long-term mortality.

Pneumococcal infections are vaccine-preventable diseases, whose global burden can be reduced by using pneumococcal vaccines. Herd immunity induced by the introduction of pneumococcal conjugate vaccines (PCV) in systematic childhood vaccination has led to a significant reduction in episodes of vaccine-type strains of IPD in all ages,^{11,12} including adults ≥ 65 years old and people with immunocompromising conditions or chronic diseases.¹² However, the rise of non-vaccine serotypes has blunted the impact of childhood vaccination in adults particularly in those ≥ 65 years old.¹¹

Herd immunity induced by universal childhood vaccination is essential to protect the elderly, chronically ill individuals and

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those with immunocompromising conditions, in which vaccine responses may be lower than those in general population. The introduction of 13-valent pneumococcal conjugate vaccine (PCV13) in children in the USA reduced IPD caused by PCV13 serotypes by 54–74% in immunocompromised individuals and by 68% in adults ≥ 65 years of age with chronic diseases.¹² However, despite indirect protection from herd immunity from childhood immunization, direct vaccination of adults is also a necessary and essential preventive measure, as demonstrated by the persistence of PCV13 serotypes in adult IPD in Spain, including serotype 3 – which has become the most frequent in people ≥ 65 years of age in 2023 – and other emerging non-PCV13 serotypes included in the 23-valent polysaccharide vaccine (PPV23) and in the new extended-valence pneumococcal conjugate vaccines, 15-valent pneumococcal conjugate vaccine (PCV15) and 20-valent pneumococcal conjugate vaccine (PCV20).¹¹

PPV23 effectiveness against IPD caused by vaccine serotypes has been consistently shown, although it varies from 30% to 70% in subjects ≥ 65 years, depending on the different studies. Besides, effectiveness could be much lower with increasing age, in subjects with comorbidities and as the time elapsed since vaccination increases.^{13,14} There is more uncertainty about the effectiveness of PPV23 against pneumonia, since although most studies have found no effectiveness, a more recent work has shown a 48–64% effectiveness for community-acquired pneumonia caused by any serotype.¹⁴

Pneumococcal conjugate vaccines (PCV), in which pneumococcal capsular polysaccharides are bound to a protein carrier, have the advantage that, unlike PPV23, generate memory B cells and secondary antibody responses after the administration of boosters, which probably translates into a greater and longer-lasting effectiveness. In addition, they reduce pneumococcal nasopharyngeal colonization by vaccine serotypes, inducing indirect or herd immunity.

Although there is little information on the effectiveness of PCV in adults, the experience with PCV7, 10-valent pneumococcal conjugate vaccine (PCV10) and PCV13 in children, which have shown excellent effectiveness for both IPD and pneumococcal pneumonia, allows us to infer that these vaccines will also have a relevant role in the control of pneumococcal infections in adults, as it has been confirmed in recent studies. In a clinical trial that included more than 85,000 patients over 65 years of age, PCV13 was 75% effective against IPD caused by vaccine serotypes and 45% effective against non-bacteremic and non-invasive community-acquired pneumonia.¹⁵ Real-life data also confirm these facts. In a case–control study, pneumococcal vaccination of persons with autoimmune inflammatory diseases reduced hospitalizations for pneumonia by 30% and pneumonia-related deaths by 40%.¹⁶ Another study with a negative test design has demonstrated an 72.8% effectiveness of PCV13 against hospitalization for community-acquired pneumonia caused by vaccine serotypes in adults over 65 years of age.¹⁷ Recently, another study has shown that PCV13 is 6.7% effective in preventing hospitalization for any type of pneumonia and 5.8% effective in preventing hospitalization for lobar pneumonia.¹⁸

There is no evidence that PCV13 is clinically effective in people with HIV infection, hematopoietic stem cell transplantation, solid organ transplantation, or other immunocompromising conditions. However, since a proportion of subjects belonging to these groups develop an immune response to PCV, albeit generally lower and more variable than general population,¹⁹ vaccination of these risk groups is also indicated.

In addition to preventing morbidity and mortality from pneumococcal infections there are some other reasons to vaccinate. In the current era, when antimicrobial resistance (AMR) poses an important global health challenge, vaccines can help mitigate the

problem.²⁰ PCV use may decrease pneumococcal resistance by both reducing antibiotic consumption and limiting the spread of non-susceptible strains of pneumococcus targeted by the vaccine. Systematic vaccination of children with PCV has led to a reduction in the use of antibiotics, and consequently to a decrease in strains not susceptible to beta-lactams antibiotics, macrolides and trimethoprim-sulfamethoxazole. Although this effect has been more noticeable in children, it has also occurred in adults. The reduction of strains not susceptible to penicillin has ranged from 40% to more than 80%, while the reduction of meningial strains not susceptible to cefotaxime has decreased by more than 80%.²⁰

Two new PCV, PCV15 and PCV20, are now available, which extend the serotypes covered by PCV13. PCV15 includes, in addition to the serotypes of PCV13, serotypes 22F and 33F. PCV20 contains serotypes 8, 10A, 11A, 12F, 15B, 22F and 23F, in addition to the serotypes common to PCV13. A new 21-valent vaccine, specifically directed to adults, which includes serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 115C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F and 35B, has been recently approved in some countries such as the USA and Canada.

There are no effectiveness studies on any of these vaccines, and their approval has been based on non-inferiority studies, compared with PCV13, on their capacity to induce specific antibodies against capsular pneumococcal polysaccharides and the opsonophagocytic activity of the serum.

Considering the properties of current pneumococcal vaccines, it seems clear that pneumococcal conjugate vaccines offer some advantages over PPV23 for vaccination in adults, such as a greater effectiveness against IPD, effectiveness against pneumococcal pneumonia, and probably a longer-lasting protection. In Spain, the preferred vaccine for pneumococcal adult vaccination is currently the 20-valent vaccine,¹¹ due to its greater coverage of circulating serotypes in adults – including some with reduced susceptibility to antibiotics – which reaches up to 65% in people ≥ 65 years.¹¹ The vaccination schedule depends on the risk circumstances of the patients and the pneumococcal vaccines that they have previously received.

In summary, the study by Serrano-Tomás et al.,¹ demonstrates the need to improve vaccination against pneumococcus in adults over 60–65 years of age and those belonging to risk groups. Nurses and doctors caring for adult patients should always keep in their mind, just as pediatric nurses and pediatricians do, the immunization schedule of the Ministry of Health²¹ to properly vaccinate old people and patients with chronic diseases or immunocompromising conditions against all vaccine-preventable diseases, such as pneumococcal infections, influenza, zoster and others. The encounters of patients with nurses and doctors should not in any case become missed opportunities for vaccination.

Conflict of interest

I declare that I have received emoluments for training activities and scientific advice from Sanofi, MSD, Pfizer and GSK.

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